

REMARKS

At the outset, Applicant would like to thank the Examiner for the recent interview with the undersigned Agent. At the interview, the contentions of the outstanding Official Action were discussed.

Claims 7-8 and 10-13 are pending in the present application. Claims 9 has been canceled. Claims 8 and 10 have been amended as independent claims.

In the outstanding Official Action, claim 9 was rejected under 35 USC §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. It is believed that the present amendment obviates this rejection.

As noted above, claim 9 has been canceled. Thus, it is believed that the claimed invention is definite to one of ordinary skill in the art.

Claims 7-11 were rejected under 35 USC §102(b) as allegedly being anticipated by RUPREHT et al. Claims 12-13 were rejected under 35 USC §103(a) as allegedly being unpatentable over RUPREHT et al. alone. These rejections are respectfully traversed.

It is believed that RUPREHT et al. fails to disclose or suggest the claimed invention. In imposing and maintaining the

rejection, the Official Action contends that RUPREHT et al. discloses treating central anticholinergic syndrom (CAS), which encompasses confusion and delirium, with the acetylcholinesterase inhibitor physotigmine.

However, anticholinergic delirium is a delirium which occurs when anticholinergically acting substances are administered. CAS is an anticholinergic delirium. As stated in the abstract of RUPREHT et al., "it occurs when central cholinergic sites are occupied by specific drugs and also as a result of an insufficient release of acetylcholine".

This stands in contrast with the present application which states that non-anticholinergically caused deliria, and post operative deliria in particular (i.e. excluding those induced by anticholinergics), either improved following administration of cholinomimetic drugs called acetylcholinesterase-inhibitors, or can be effectively prevented by the use of acetylcholinesterase-inhibitors.

Indeed, the RUPREHT et al. abstract describes CAS as a disorder wherein the patient exhibits symptoms of confusion and peripheral signs of hypofunction or blockage of a cholinergic system (dry mouth, dry skin, tachycardia, vision problems, dysuria). CAS cannot be equated to delirium (acute confusion) since there must be other indications of anticholinergic origin of the mental state. Thus, RUPREHT et al. teach that the

pathogenesis of CAS is attributable to the blockage of cholinergic cites by substances, or by intoxication by other substances which cause a reduced release of acetylcholine, and therefore act in an anticholinergic manner.

As evidence of this assertion, the Examiner's attention is respectfully directed to 37 CFR §1.132 declaration by Dr. Peter Fischer and the article cited therein. The declaration explains that CAS is an anticholinergic delirium that RUPREHT et al. does not disclose or suggest the claimed invention.

As a result, it is believed that RUPREHT et al. fails to anticipate or render obvious the claimed invention.

In the outstanding Official Action, claims 7-13 were rejected under 35 USC §103(a) as allegedly being unpatentable over ENZ in view of OSHIRO et al. this rejection is respectfully traversed.

Once again, Applicants note that the present invention relates to a method of treating delirium, caused neither by anticholinergic intoxication nor by degeneration of the cholinergic system. ENZ is directed to a cholinesterase inhibitor and teaches that cholinesterase inhibitors are used for treatment of a variety of disorders such as senile dementia, Alzheimer's disease, Huntington's chorea tardive dyskiasias, hyperkinesias, mania, acute confusion disorder, Downs syndrome,

and Friedrich ataxia. As, it is believed that the ENZ patent is directed to indications of anticholinergic related disorders.

In an effort to remedy the deficiencies of ENZ, the outstanding Official Action cites to OSHIRO et al. However, OSHIRO et al. relate to patients with awareness disorders. OSHIRO et al. do not relate to patients with fluctuating consciousness disorders nor to acute disorders and fails to disclose or suggest a method for treating delirium, caused either by anticholinergic intoxication nor by degeneration of the cholinergic system, in a patient.

Thus, it is believed that the proposed combination of ENZ in view of OSHIRO et al. fails to render obvious the claimed invention.

Thus, in view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 7-8 and 10-13, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

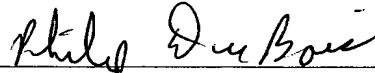
The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

Application No. 09/856,352  
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Reply to Office Action of March 13, 2003  
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overpayment to Deposit Account No. 25-0120 for any additional  
fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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**APPENDIX:**

The Appendix includes the following item(s):

- a 37 CFR 1.132 Declaration
- article: *Postoperative delirium in the elderly*, 1994; 73:  
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